group of human volunteers on a diet consisting of polished rice, patent white flour, farina, cane sugar, lard, butter, and lean beef, having a total daily food value of 1960 calories. To this was added 200 gm. of dehydrated raw egg white with a caloric value of 928, plus adequate supplementary amounts of thiamin chloride, riboflavin, nicotinic acid, vitamin A, ferrous sulphate and calcium lactate.

After about three weeks on this diet all volunteers developed a fine scaly desquamation of the skin, which however disappeared spontaneously in seven to ten days. During the seventh and eighth weeks all subjects showed a pronounced grayish pallor of the skin and mucous membranes, with a return of the fine branny desquamation by the ninth week. Mild depression progressing to extreme lassitude, somnolence, and mild panic state was noted in most subjects, accompanied by muscular pains, hyperesthesia, localized paresthesias, anorexia and occasional nausea. There was a definite diminution in the hemoglobin content of the blood, a striking rise in serum cholesterol, and a marked diminution in biotin excretion in the urine. The four subjects excreted an average of about 5 micrograms of biotin daily, as compared with their previous excretion of 40 micrograms.

Vitamin therapy was begun on the tenth week. This took the form of a daily injection of 150 micrograms of commercial biotin concentrate. Within 3 to 5 days after beginning this therapy the depression, muscular pains, precordial distress and anorexia were abolished, the ashy pallor of the skin disappeared, the serum cholesterol was reduced to normal and the daily urinary excretion rose to 55 micrograms biotin. Sydenstricker and his coworkers conclude from these results that human volunteers, maintained on diets containing adequate amounts of vitamins, iron and calcium, may develop "spontaneous avitaminosis," if approximately a third of the daily caloric intake is supplied by dessicated egg white. As in lower animals this apparent egg-white toxicity is presumably due to gastro-intestinal conjugation of biotin with "avidalbumin" or "avidin," which functions as an "anti-biotin."

It has long been a practice of poultry raisers to add charcoal to poultry feeds, under the impression that charcoal adsorbs bacterial toxins and other putrefactive products, and thus improves health and reduces mortality. Almquist and Zander[6] of the University of California, however, have shown that the addition of 2 per cent charcoal to a basal diet, containing adequate (but not excessive) amounts of all necessary vitamins, almost invariably leads to a somewhat similar "spontaneous avitaminosis." Stunted growth, "curled-toe paralysis," incoördinations, multiple subcutaneous hemorrhages, prolonged clotting time and eroded gizzard lining are among the manifestations noted in charcoal-fed chicks, pointing to a multiple avitaminosis. This deduction was confirmed therapeutically, since each of these manifestations was prevented or cured on the oral administration of the appropriate vitamin, or by changing to a commercial mash containing a considerable excess of this vitamin. Presumably charcoal has the property of adsorbing numerous vitamins from the gastro-intestinal contents, thus preventing adequate vitamin adsorption from the intestinal contents.

Thus far the phenomenon of gastro-intestinal fixation or inactivation of vitamin has been of little clinical interest except in cases of prolonged and habitual use of mineral oil laxatives. It was shown by Burrows and Farr[7] that the addition of as little as 1.3 per cent mineral oil to a well-balanced diet causes lethal vitamin A deficiency in rats, death taking place in about three weeks. There is also[8] adequate evidence of an intestinal inactivation of vitamin D. Demonstration that an excessive diet of raw eggs may be equally deleterious is therefore of suggestive clinical interest.

In order to prevent popular misconception, however, it might be well to emphasize the fact that adequate cooking destroys the "avidin" or "anti-biotin" in raw egg, and that its apparent "toxicity" is readily prevented by such biotin-rich foods as cabbage, spinach, liver, kidney and cow's milk. It is known that egg yolk is very rich in biotin, but unfortunately it contains only half the amount of this essential vitamin necessary to neutralize the "avidin" or "anti-biotin" in the accompanying egg albumin.[9]

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## IMMUNOLOGIC EFFECTS OF SYMPATHECTOMY

After a year's wartime delay, studies of the effects of total sympathectomy on natural immunity and specific antibody formation in animals have been reported by Went and Lissak[1] of the Physiological Institute, Debrecen University, Hungary.

For two decades the rôle of the nervous system in specific allergic and immune reactions has been of theoretic interest. Experimental evidence has been reported by European investigators, suggesting the existence of a specialized "immunity

center" in the brain, initiating or coördinating specific antibody formation. Schamburow[2] of the Moscow Clinical Institute injected E. coli and E. typhosa vaccines into the anterior chamber of the right eye of rabbits, and reported a local synthesis of specific agglutinins in the injected eye, with their "reflex" synthesis in the opposite eye. In many of his rabbits only a trace of agglutinin was demonstrable in the blood stream with many multiples of this amount in the non-injected eye. He translated these data as proof of a reflex local antibody synthesis by non-vaccinated tissues, presumably through a hypothetical "immunity center."

Although his alleged "reflex ocular immunity" could not be confirmed by American investigators,[3] the probable rôle of the sympathetic nervous system in specific antibody formation has been quite generally affirmed. As early as 1898, Salomonsen and Madsen[4] demonstrated a marked increase in antitoxin titer in horses as a result of the administration of parasympathetic stimulants (pilocarpin). Joachimoglu and Wada[5] afterwards reported the opposite effect, a reduction in specific agglutinin production in rabbits as a result of the administration of parasympathetic depressants (atropin). In a recent summary of accumulated data Belák[6] concluded that in their relationship to the autonomic nervous system antibodies can be divided into two groups: (i) a "sympathogenic group," including complement and normal opsonins, which are favored by sympathetic stimulants and inhibited by the parasympathetic, and (ii) a "parasympathogenic group," including antitoxins, precipitins, and bacteriolysins, which have the opposite relationship, being favored by the parasympathetic stimulants and inhibited by the sympathetic.

This division of antibodies into two neurogenic groups was of little practical interest at the time. With the development of the modern surgical practice of regional sympathectomy, however, the theory became of practical clinical value. The experimental evidence in support of the neurogenic theory of immunity was, therefore, reëxamined by the Hungarian physiologists. They found the pharmacologic evidence inconclusive due to the presumptive direct toxic action of atropin, pilocarpin, etc., on antibody-forming tissues. To obtain conclusive evidence, Went and Lissák performed total sympathectomy on a group of cats, the operation being performed in several stages by the Cannon[7] technique. Four to six weeks after complete recovery from the last stage of the operation, blood samples were titrated for complement and bactericidal power, E. coli being used as the test organism. Control titrations were made with an equal number of non-operated cats. Within the limits of the experimental error, the complement and colicidal titers were identical in the two groups. From this it was evident that the integrity of the sympathetic nervous system is not essential for the production and maintenance of normal serum titer. Alterations of serum titer reported by previous investigators as a result of the administration of sympathetic stimulants or depressants are presumably due to direct toxic action on extra-neural tissues.

The same group of sympathectomized cats was afterwards tested for their ability to synthesize specific antibodies. Foreign proteins and nonviable bacterial vaccines were injected into these cats, with control injections into an equal number of normal cats. With the limited number of sympathectomized animals for such tests, no qualitative or quantitative differences were demonstrable between their power to synthesize antibodies and the production of the same antibodies in normal controls. From this they concluded that the sympathetic nervous system plays no rôle in the production or coördination of acquired humoral immunity.

Their data suggest that regional sympathectomy is without deleterious effect on natural or acquired immunity, and would be of no benefit in regional anaphylaxis. It should be emphasized, however, that their studies were confined to the humoral factors in immunity and anaphylaxis. With the obsolescence of the Ehrlich side-chain theory[8] it is no longer axiomatic that humoral and cellular chemical defenses are either qualitatively or quantitatively identical. Effect of sympathectomy on fixed tissue defense is still an open question.

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## MALPRACTICE PROPHYLAXIS

It is fundamental that every patient be cared for with meticulous attention to the requirements of good medical practice. This comprehends sufficiency of investigation, observation and treatment; utilization of every indicated laboratory aid; protection of those coming in contact with the patient; instruction, when necessary, of the patient and of those caring for the patient, so that all things needed may be carried out during the absence of the attending physician; recognition of the importance of psychological